CLAIMS

1. An isolated nucleic acid molecule from a nonchromoprotein enediyne biosynthetic gene cluster from *Micromonospora echinospora* comprising said nucleic acid molecule, a portion or portions of said nucleic acid molecule wherein said portion or portions encode a protein or proteins, a portion or portions of said nucleic acid molecule wherein said portion or portions encode a biologically active fragment of a protein or proteins, a single-stranded nucleic acid molecule derived from said nucleic acid molecule, or a single-stranded nucleic acid molecule derived from a portion or portions of said nucleic acid molecule.

2. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule comprises at least one of *cal*A, *cal*B, *cal*C, *cal*D, *cal*E, *cal*F, *cal*G, *cal*H, *cal*I, *cal*J, *cal*K, *cal*L, *cal*M, *cal*N, *cal*O, *cal*P, *cal*Q, *cal*R, *cal*S, *cal*T, *cal*U, *cal*V, *cal*W, *cal*X, *6MSAS, ActI, ActII, ActIII, orf1, orf2, orf3, orf4, orf5, orf6, orf7, orf8, orfI, orfII orfIII, orfIV orfV, orfVI, orfVII, orfVIII, orfIX, orfX, orfXI,* or an IS-element gene.

3. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes two or more proteins.

4. The isolated nucleic acid molecule of Claim 1, wherein said molecule comprises a complete nonchromoprotein enediyne biosynthetic gene cluster.

5. The isolated nucleic acid molecule of Claim 1, wherein said nonchromoprotein enediyne is calicheamicin.

6. An isolated nucleic acid molecule capable of hybridizing with a nucleic acid molecule from *Micromonospora echinospora* spp. *calichensis*, wherein said

nucleic acid molecule from *Micromonospora echinospora* spp. *calichensis* encodes one or more proteins from a nonchromoprotein enediyne biosynthetic gene cluster.

7. The isolated nucleic acid molecule of Claim 6, wherein said molecule encodes a protein having the activity of at least one protein from said nonchromoprotein enediyne biosynthetic gene cluster.

8. The isolated nucleic acid molecule of Claim 6, wherein said nucleic acid molecule comprises at least one of *cal*A, *cal*B, *cal*C, *cal*D, *cal*E, *cal*F, *cal*G, *cal*H, *cal*I, *cal*J, *cal*K, *cal*L, *cal*M, *cal*N, *cal*O, *cal*P, *cal*Q, *cal*R, *cal*S, *cal*T, *cal*U, *cal*V, *cal*W, *cal*X, *6MSAS, ActI, ActII, ActIII, orf*1, *orf*2, *orf*3, *orf*4, *orf*5, *orf*6, *orf7*, *orf8*, *orfI*, *orfII orfIII, orfIV orfV*, *orfVI*, *orfVII, orfVIII, orfIX*, *orfX*, *orfXI* or an IS-element gene.

9. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.1.

10. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.3.

11. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.5.

12. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.7

13. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.9

14. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.11

15. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.13

16. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.15

17. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.17

18. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.19

19. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.21

20. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.23

21. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.25

22. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.27

23. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.29

24. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.31

25. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.33

26. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.35

27. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.37

28. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.39

29. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.41

30. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.43

31. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.45

32. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.47

33. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.49

34. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.51

35. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.53

36. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.55

37. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.57

38. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.59

39. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.61

40. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.63

41. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.65

42. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.67

43. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.69

44. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.71

45. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.73

46. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.75

47. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.77

48. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.79

49. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.81

50. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.83

51. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.85

52. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.87

53. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.89

54. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.91

55. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.93

56. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.94

57. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a P_{450} oxidase from *Micromonospora echinospora* spp. *calichensis*.

SUB A2 CONT.

58. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a membrane transporter from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

59. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an *O*-methyltransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

60. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a glycosyltransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

61. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a *N,N*-dimethyltransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

62. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a dipeptide transporter from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

63. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a L-cysteine/cystine C-S-lyase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

64. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an oligopeptide transporter protein from a gene cluster of

Micromonospora echinospora spp. *calichensis* coding for calicheamicin biosynthesis.

65. The isolated nucleic acid molecule of Claim 1, which encodes a polypeptide encoding for a regulatory protein from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

66. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a hexopyranosyl-2-3-reductase from *Micromonospora echinospora* spp. *calichensis*.

67. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a desaturase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

68. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an UDP-D-glucose 6-dehydrogenase from *Micromonospora echinospora* spp. *calichensis*.

69. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a transcriptional regulator from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

70. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an oxygenase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

71. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a halogenase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

72. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a β-keto-acyl synthase III from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

73. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a cytochrome P450 from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

74. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a TDP-4-keto-6-deoxy-L-hexose 2,3-dehydrogenase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

75. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an orsellenic acid synthase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

76. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a polyketide cyclase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

77. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a polyketide synthase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

78. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an integrase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

79. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a chromosome partitioning protein from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

80. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a hydroxylase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

81. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an aminotransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

82. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a glu-ammonia-ligase adenylyltransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

83. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a methyltransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

84. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an integral membrane protein from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

85. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a membrane protein from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

86. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an immunity resistance protein from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

87. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an insertional element from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

Sub B12

88. An expression vector comprising a nucleic acid molecule encoding a protein or biologically active fragment of a protein, wherein said nucleic acid molecule is a nucleic acid molecule of Claim 1.

89. The expression vector of Claim 88, wherein said nucleic acid molecule is operably linked to regulatory sequences to control expression of said protein or polypeptide.

90. The expression vector of Claim 89, wherein the regulatory sequence is a *Streptomyces* promoter.

Sub B13

91. A host cell transformed with the nucleic acid molecule of Claim 1.

92. A host cell transformed with the expression vector of Claim 88.

93. A host cell transformed with the expression vector of Claim 89.

94. The host cell of Claim 91, wherein said host cell is a bacterium, yeast, insect, plant, fungi, or mammalian cell.

95. The host cell of Claim 91, wherein the host bacteria is *E. coli* or *Streptomyces*.

96. A cosmid comprising an isolated nucleic acid molecule from a nonchromoprotein enediyne biosynthetic gene cluster from *Micromonospora echinospora*, wherein said isolated nucleic acid molecule comprises said nucleic acid molecule, a portion or portions of said nucleic acid molecule wherein said portion or portions encode a protein or proteins, a portion or portions of said nucleic acid molecule wherein said portion or portions encode a biologically active fragment of a protein or proteins, a single-stranded nucleic acid molecule derived from said nucleic acid molecule, or a single-stranded nucleic acid molecule derived from a portion or portions of said nucleic acid molecule.

97. The cosmid of Claim 96, wherein said nucleic acid molecule comprises at least one of *cal*A, *cal*B, *cal*C, *cal*D, *cal*E, *cal*F, *cal*G, *cal*H, *cal*I, *cal*J, *cal*K, *cal*L, *cal*M, *cal*N, *cal*O, *cal*P, *cal*Q, *cal*R, *cal*S, *cal*T, *cal*U, *cal*V, *cal*W, *cal*X, *6MSAS, ActI, ActII, ActIII, orf*1, *orf*2, *orf*3, *orf*4, *orf*5, *orf*6, *orf*7, *orf*8, *orfI, orfII orfIII, orfIV orfV, orfVI, orfVII, orfVIII, orfIX, orfX, orfXI* or an IS-element gene.

98. A method of expressing a protein comprising the steps of transfecting a host cell with the expression vector of Claim 88 and incubating said cell for a length of time and under conditions sufficient for expression of a desired quantity of said protein or said biologically active fragment of a protein.

99. The method of Claim 97, wherein said host cell is a bacterium, yeast, insect, plant, fungi, or mammalian cell.

100. A method of purifying calicheamicin using affinity chromatography, comprising the steps of exposing a solution containing calicheamicin to an affinity column having CalC bound thereto, and recovering calicheamicin.

101. A polypeptide comprising amino acid sequence SEQ ID. No.: 2.

102. A polypeptide comprising amino acid sequence SEQ ID. No.: 4.

103. A polypeptide comprising amino acid sequence SEQ ID. No.: 6.

104. A polypeptide comprising amino acid sequence SEQ ID. No.: 8.

105. A polypeptide comprising amino acid sequence SEQ ID. No.: 10.

106. A polypeptide comprising amino acid sequence SEQ ID. No.: 12.

107. A polypeptide comprising amino acid sequence SEQ ID. No.: 14.

108. A polypeptide comprising amino acid sequence SEQ ID. No.: 16.

109. A polypeptide comprising amino acid sequence SEQ ID. No.: 18.

110. A polypeptide comprising amino acid sequence SEQ ID. No.: 20.

111. A polypeptide comprising amino acid sequence SEQ ID. No.: 22.

112. A polypeptide comprising amino acid sequence SEQ ID. No.: 24.

113. A polypeptide comprising amino acid sequence SEQ ID. No.: 26.

114. A polypeptide comprising amino acid sequence SEQ ID. No.: 28.

115. A polypeptide comprising amino acid sequence SEQ ID. No.: 30.

116. A polypeptide comprising amino acid sequence SEQ ID. No.: 32.

117. A polypeptide comprising amino acid sequence SEQ ID. No.: 34.

118. A polypeptide comprising amino acid sequence SEQ ID. No.: 36.

119. A polypeptide comprising amino acid sequence SEQ ID. No.: 38.

120. A polypeptide comprising amino acid sequence SEQ ID. No.: 40.

121. A polypeptide comprising amino acid sequence SEQ ID. No.: 42.

122. A polypeptide comprising amino acid sequence SEQ ID. No.: 44.

123. A polypeptide comprising amino acid sequence SEQ ID. No.: 46.

124. A polypeptide comprising amino acid sequence SEQ ID. No.: 48.

125. A polypeptide comprising amino acid sequence SEQ ID. No.: 50.

126. A polypeptide comprising amino acid sequence SEQ ID. No.: 52.

127. A polypeptide comprising amino acid sequence SEQ ID. No.: 54.

128. A polypeptide comprising amino acid sequence SEQ ID. No.: 58.

129. A polypeptide comprising amino acid sequence SEQ ID. No.: 60.

130. A polypeptide comprising amino acid sequence SEQ ID. No.: 62.

131. A polypeptide comprising amino acid sequence SEQ ID. No.: 64.

132. A polypeptide comprising amino acid sequence SEQ ID. No.: 66.

133. A polypeptide comprising amino acid sequence SEQ ID. No.: 68.

134. A polypeptide comprising amino acid sequence SEQ ID. No.: 80.

135. A polypeptide comprising amino acid sequence SEQ ID. No.: 82.

136. A polypeptide comprising amino acid sequence SEQ ID. No.: 84.

137. A polypeptide comprising amino acid sequence SEQ ID. No.: 86.

138. A polypeptide comprising amino acid sequence SEQ ID. No.: 88.

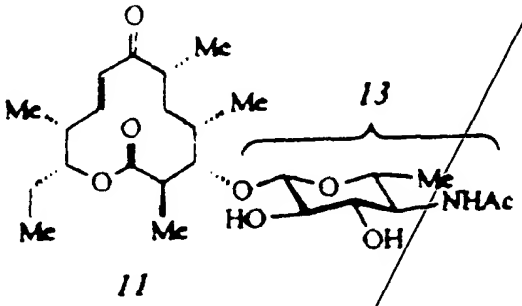
139. A polypeptide comprising amino acid sequence SEQ ID. No.: 90.

140. A polypeptide comprising amino acid sequence SEQ ID. No.: 92.

141. A polypeptide comprising amino acid sequence SEQ ID. No.: 95.

142. A method of conferring calicheamicin resistance on a subject comprising the steps of obtaining cells from the subject, transforming the cells with a calicheamicin self resistance gene, and returning the cells to the subject.

143. A compound having the structure:



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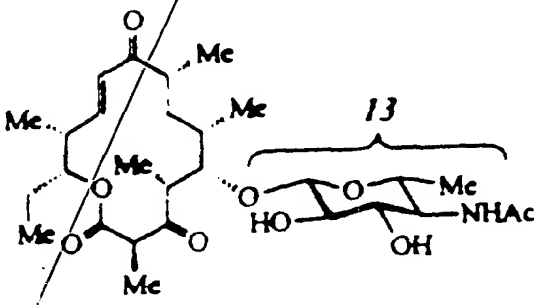
144. A compound having the structure:



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145. The isolated nucleic acid molecule of claim 1, wherein said protein comprises at least one of amino acid sequence SEQ ID Nos.: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20,

22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, or 95.

146. The isolated nucleic acid molecule of claim 1, wherein said biologically active fragment of a protein comprises a biologically active portion of at least one of amino acid sequence SEQ ID Nos.: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, or 95.

147. A polypeptide comprising amino acid sequence SEQ ID. No.: 56.

148. An isolated nucleic acid molecule comprising at least one of the nucleotide sequences of SEQ ID Nos. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 , or 94, or a portion of portions thereof or an allele or alleles thereof, wherein said isolated nucleic acid molecule encodes a biologically functional protein or portion of a protein.

149. A polypeptide comprising the amino acid sequence of at least one of SEQ ID Nos. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, or 95, or a functional variant of one or more of those polypeptides.